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Being Born Under Adverse Economic Conditions Leads to a Higher Cardiovascular Mortality Rate Later in Life: Evidence Based on Individuals Born at Different Stages of the Business Cycle

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Abstract We connect the recent medical and economic literatures on the long-run effects of early-life conditions by analyzing the effects of economic conditions on the individual cardiovascular (CV) mortality rate later in life, using individual data records from the Danish Twin Registry covering births since the 1870s and including the cause of death. To capture exogenous variation of conditions early in life, we use the state of the business cycle around birth. We find significant negative effects of

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economic conditions around birth on the individual CV mortality rate at higher ages. There is no effect on the cancer-specific mortality rate. From variation within and between monozygotic and dizygotic twin pairs born under different conditions, we conclude that the fate of an individual is more strongly determined by genetic and household-environmental factors if early-life conditions are poor. Individual-specific qualities come more to fruition if the starting position in life is better.

Keywords Longevity · Genetic determinants · Health · Recession · Developmental origins

Introduction

In many scientific disciplines, the interest in long-run effects of early-life conditions has been strongly increasing. In medical science, the developmental origins and fetal programming hypotheses, which state that certain diseases at older ages can be caused by deprivation *in utero* or around birth, have been confirmed by a range of studies; this is particularly true for cardiovascular diseases (CVD) (see references in this section). The search for early origins as causes of CVD later in life has become an important focal point of research in medical science. In epidemiology and demography, various indicators of early-life conditions have been found to be associated with health and mortality later in life. At the same time, economists and sociologists are increasingly interested in the importance of parental income and socioeconomic status as explanations for health later in life.[1]

In this article, we aim to combine the medical/epidemiological and economic contributions on long-run effects of early-life conditions by analyzing the causal effect of economic conditions around birth on the individual rate of mortality attributable to cardiovascular diseases much later in life. For this purpose, we use individual twin register data covering multiple birth cohorts and containing the dates of birth and death and the cause of death.

In each of the aforementioned disciplines, the empirical evidence often relies on indicators of early-life conditions for which it is questionable that they are exogenous causal determinants of health later in life. An association between such an indicator and health later in life then does not necessarily imply the presence of a causal effect of early-life conditions. Instead, the indicator and the health outcome may be jointly affected by related unobserved determinants. Consider, for example, parental income or wealth at birth. To some extent, parental income and wealth at birth are determined by unobserved factors that also directly affect the morbidity and

[1] Surveys and meta-studies of the epidemiological and medical evidence of associations of birth weight indicators and CVD later in life have been published in Huxley et al. (2007), Poulter et al. (1999), and Rasmussen (2001). The survey in Eriksson (2007) also focuses on medical early-life indicators measured after birth. Gluckman et al. (2005) and Barker (2007) give overviews of the underlying medical mechanisms. Some studies also point to long-run effects on other diseases, such as Type 2 diabetes and breast cancer. Pollitt et al. (2005) provide a survey and meta-study of the life course literature on causal pathways in which early-life socioeconomic status (SES) is associated with CV morbidity and mortality later in life. Galobardes et al. (2004) survey studies on early-life SES and cause-specific mortality in adulthood. See also Case et al. (2005) and Case et al. (2002) and references therein for influential studies focusing on economic household conditions early in life.

mortality of individuals at higher ages. An association between parental income at birth and longevity may then be due to the fact that these have shared determinants. Similar problems arise with the use of birth weight or weight at gestational age, as has been acknowledged in the medical and epidemiological literature. These measures depend on genetic determinants, and it is not clear to what extent these can be controlled for by conditioning on additional covariates (see arguments made in, for example, the surveys of Huxley et al. 2007; Lawlor 2008; Poulter et al. 1999; and Rasmussen 2001; see also Ben-Shlomo 2001; Järvelin et al. 2004).

We deal with this methodological problem by using the state of the business cycle at early ages as indicators of early-life conditions. Transitory macroeconomic conditions during pregnancy of the mother and early childhood are unanticipated and exogenous from the individual point of view, and they affect income for many households. In a recession, the provision of sufficient nutrients and good living conditions for infants and pregnant women may be hampered, and the stress level in the household may be higher. It can be argued that the only way in which the indicators can plausibly affect old-age mortality is by way of the individual early-life conditions; in the second section, we address this in more detail. The use of transitory features of the macroenvironment as indicators of individual early-life conditions, rather than unique characteristics of the newborn individual or his or her family or household, has recently become popular. Doblhammer (2004) used month of birth, whereas other studies compared individuals born during extreme events, such as epidemics, wars, and famines, with those born outside the periods covered by these events (see, e.g., Almond 2002). Bengtsson and Lindström (2000, 2003) used the transitory component of the local price of rye around birth and the local infant mortality rate. Van den Berg et al. (2006) examined the state of the business cycle at early ages as determinants of all-cause individual mortality, using Dutch data on births during 1815–1902. Cutler et al. (2007) looked at the Great Depression in the Dust Bowl area in the United States.[2] One may argue that results based on extreme events are hard to extrapolate because long-run effects of these events may be nonlinear with the hardships early in life. This makes business cycles and seasons potentially more useful as indicators of early-life conditions than severe epidemics or famines. Moreover, extreme events may lead to high infant mortality and dynamic selection of the fittest in the cohort, which complicates the statistical analysis.

The Danish Twin Registry data that we use in the present article are uniquely equipped for our purposes because (1) they contain the exact dates of birth and death; (2) they cover birth cohorts over a rather large time frame, spanning many transitory fluctuations in the economy; (3) in each birth cohort that we consider, they include a sufficiently large fraction of individuals who died; and (4) they contain the cause of death. Other data sets like those in the Human Mortality Database contain death-cause information for only recent birth cohorts in which most individuals are

[2] They addressed CVD as one of the outcomes. Based on interviews that were conducted every two years beginning in 1992, they did not find evidence of a long-run effect on CVD among those who survived until 1992. One explanation the authors offered is that deaths due to CVD between interview dates may be underreported. This suggests that registered causes of death may be more informative about long-run CV effects than self-reported health statuses. Another explanation they posited is that there may have been sufficient opportunities for consumption smoothing, and sufficient relief payments, to mitigate adverse effects of this recession.

still alive (see, e.g., Andreev 2002, for Danish data). Alternatively, birth dates in data sets are time aggregated into intervals spanning more than a year, which is fatal for our approach; they contain only a small number of birth cohorts around some extreme event; and/or they contain health outcomes but not mortality outcomes.

A fifth and major additional advantage of the twin data is that the observation of zygosity of the twin pair allows us to assess the relative importance of genetic factors, shared environmental factors, and individual-specific factors as determinants of CV mortality and longevity. More specifically, we can assess the extent to which the relative importance of family-/household-specific and individual-specific determinants depends on the business cycle at birth and thus on economic conditions early in life. From this, we can infer whether the fate of an individual born under adverse conditions is more strongly shaped by the family background *vis-à-vis* the individual's own characteristics than if he or she were born under better conditions. As noted earlier, we address the presence of such interactions by using transitory exogenous indicators of economic conditions early in life, which is a methodological advantage over the use of family income or social status as an interacting variable for genetic determinants.

One may argue that a twin birth poses a heavier burden on the household than the birth of a single child. This merely means that the exogenous variation in early-life conditions will be expressed more strongly through twins, but it obviously does not affect the existence or nonexistence of the causal effect from these conditions. In this sense, a twin birth in a mild recession should have the same effect as a single birth in a sufficiently severe recession. Another issue is whether the composition of the (twin) birth cohorts systematically varies over the business cycle. We investigate this by examining fluctuations in birth rates and twinning rates, and by using additional survey data on the composition.

Long-run effects of economic conditions early in life may work through nutrition, disease exposure, household stress levels, and the level of living comfort in the household. We shed light on these by studying the importance of the timing of the fluctuations in economic conditions around the date of birth and by interacting the effects with spatial indicators. Specifically, we examine the relative importance of the different months of pregnancy, the date of birth, and the months and years adjacent to the moment of birth, and we relate spatial variation in the effects to spatial differences in health infrastructure as documented in the historical literature on Denmark.

We also consider effects on other death causes (such as cancer and infectious diseases) and on subsets of the CV category (such as ischemic heart diseases and strokes). These additional novel analyses will also be compared with the medical and demographic evidence to date. They also demonstrate the extent to which effects on overall mortality are driven by CVD.

The Danish twin data have been used by many other studies, which have often exploited or investigated the similarities between monozygotic (MZ) and dizygotic (DZ) twins (for overviews, see Harvald et al. 2004; and Skytthe et al. 2002). Christensen et al. (1995, 2001) compared patterns of (cause-specific) mortality across age and cohort intervals in the twin data to the corresponding intervals in the general population; they concluded that among adults, the patterns are usually the same. Wienke et al. (2001) replicated this comparison for coronary heart disease, and

they reached the same conclusion. See Vågerö and Leon (1994) for similar conclusions based on Swedish twin data. This body of work suggests that twins are not necessarily different from single births when it comes to the mortality distribution at higher ages. See Christensen and McGue (2008) for a discussion of the similarities between twins and single births in a wider context. The evidence for the similarities is not necessarily in conflict with the fact that twins generally have low birth weight. The nature of twins' low birth weight seems to be fundamentally different from the low birth weight experienced by some singletons. Different reference values should be used for twins and singletons because otherwise, only singletons display an association between low birth weight and long-run outcomes (see Christensen and McGue 2008; Lawlor et al. 2004; and references therein).

It should be emphasized that living conditions in Denmark around 1900 were relatively good in comparison with most other countries at the time and in comparison with many developing countries today. Life expectancy was the highest in the world (Johansen 2002a). Health insurance coverage was high. Denmark arguably had the best health care system in the world in terms of well-being of mothers and infants (see Løkke 2007 for a detailed survey). Insurance societies paid sickness absence benefits to employed workers who had fallen ill. In general, there was an extensive system of poor relief.

Nevertheless, one may conjecture that nutritional conditions in Denmark approximately 100 years ago were different from current conditions. In this respect, recent medical research has shown that not only is fetal malnourishment associated with long-run effects on CVD outcomes but that more generally discrepancies between early-life conditions *in utero* and shortly after birth on the one hand, and later lifestyle on the other hand, lead to long-run effects on CVD outcomes (see, e.g., Holemans et al. 2002 and Mogren et al. 2001; see also Fogel 1997 for an overview). In this sense, our study may also be of importance for modern societies. Individuals born in low-income households who have very high nutritional intakes later in life may be particularly at risk for adverse CVD outcomes at higher ages.[3]

For current developing countries, which in certain aspects could be regarded as similar to or worse off than Denmark in the period evaluated in the present article, the literature has focused on inequalities in infant and child mortality by household socioeconomic status because there are typically no long-run data registers (see Sastry 2004). In this sense, we aim to complement these studies by studying long-run mortality effects.

The article is organized as follows. The second section presents the data and discusses variables that we use in the analyses. The third section displays readily observable sample features that confirm the existence of the causal mechanisms that we are interested in. The fourth section describes the formal empirical analyses and the results; in this section, we also examine whether the composition of mortality determinants among newborns and newborn twins varies over the cycle in a systematic way. The fifth section offers conclusions.

[3] The virtual disappearance of infant mortality implies that those who would have died if born under adverse conditions in the nineteenth century survive into adulthood if born in current times. This can be seen as a factor that contributes to the potential relevance of long-run effects in modern societies.

Data

Individual Records from the Twin Registry

Our individual data records are derived from the Danish Twin Registry. This registry has been created over decades in an attempt to obtain a comprehensive sample of all same-sex twins born since 1870 and surviving as twins until at least age 6; it also includes many opposite-sex twins. We refer to studies listed in the opening section for detailed descriptions of the registry and the way it has been collected. A number of factors determine the selection that we use for the empirical analysis. Most importantly, we restrict ourselves to twins for whom sufficient information is available on the most important variables. A crucial aspect is that most individuals born in the chosen birth interval should be observed to die. In recent cohorts, almost all individuals are still alive, so these would merely add right-censored drawings from the lifetime duration distribution.

In the late nineteenth century, the Danish economy had a large agricultural sector, accounting for almost one-half of gross domestic product (GDP) and the workforce, but this sector itself had, to some extent, already been industrialized. The economy was open, and export volume and the business cycle were sensitive to events in Britain (for details of the Danish economy in the late nineteenth century, see, e.g., Christensen 1985; Greasley and Madsen 2006; Henriksen and O'Rourke 2005; Johansen 1985; and Statistics Denmark 1902). For our purposes, it is important to point out that unemployment benefits were introduced in Denmark in 1907, with the explicit objective of dampening adverse effects of the business cycle on the economic well-being of the Danish population. To keep the heterogeneity in early-life societal conditions within bounds, we therefore restrict attention to those born before 1907. In any case, it turns out that our results are not sensitive with respect to small changes in the cut-off year.

We restrict attention to same-sex twin pairs with known zygosity, for which both twins survive until at least January 1, 1943. This selection is made because for this group, the highest efforts have been made to collect the death cause and date. In the registry, the death cause is unobserved for all deaths before 1943, and the death cause and date are unobserved for most deaths of opposite-sex twin pairs or twin pairs with unknown zygosity after 1943. Finally, we delete births in 1870–1872 because the macroeconomic indicator (see below) seems to be unreliable for those years. The latter reduces the sample size by only 2%.

As a result, we use a sample of all 6,050 same-sex twin members with known zygosity, born during 1873–1906, for which both twins survive until at least January 1, 1943. The birth and death dates and the resulting individual lifetime durations are observed in days. The observation window ends on January 6, 2004, so that individuals still alive then (4%) have right-censored durations. Online Resource 1 gives some sample statistics. We should emphasize that the death date is observed for more than 95% of the individuals in our sample; and for 99% of the latter, we also observe the death cause. The death cause is classified according to the International Classification of Diseases (ICD), revisions 5 to 10, at the three-digit level. These are aggregated into 12 classes, from which we obtain the "cardiovascular" and "cancer" death-cause categories as well as the categories and CVD

subcategories that we analyze later in the article in the section Effects for the Other Death Causes. "Cardiovascular" concerns death from cardiovascular malfunctions and diseases, including strokes. "Cancer" concerns death from malignant neoplasms and congenital malformations, the latter of which concerns less than 0.1% of our sample. Not included in these two categories are deaths from tuberculosis; other infectious diseases; diseases of the respiratory, digestive, or urogenital system; suicide; and accidents. The "cardiovascular" death cause is the most prominent in our sample. Its frequency decreases as a function of the birth year. Among those born in the 1870s, 60% are observed to die from CVD, whereas among those born in the 1900s, this figure is 50%.[4]

When we select explanatory variables for individual mortality from the individual records, we restrict attention to characteristics that are realized at birth as opposed to later in life because the latter may be endogenous or confounded. In particular, we do not include variables on life events, such as marriage.

The information on the location of birth is two dimensional and aggregated. We observe in which of the four main parts of Denmark the individual is born: Copenhagen; Zealand, excluding Copenhagen but including the islands of Lolland and Bornholm; Funen; or Jutland, which is the only part of the country belonging to mainland Europe. We also observe a crude indicator of the degree of urbanization, distinguishing between Copenhagen, other towns (about 80), and rural areas. Currently, less aggregated information is not yet available.

Business-Cycle Data

As mentioned in the introduction, we use the business cycle as an exogenous indicator of early-life conditions. To appreciate the methodology, consider first the national annual per capita GDP in constant prices. One could compare an individual born in an era with high GDP with an otherwise identical individual born in an era with low GDP. However, a prolonged era with a high GDP leads to innovation and investment in hygiene and health care, which decreases mortality later in life for those born in this era. These are secular improvements in life conditions over time, and they make this approach uninformative on effects of individual early-life conditions. A related practical complication is that GDP displays a strong positive trend over time. A high GDP level at birth implies a high GDP level throughout life. An empirical analysis that tries to take this into account by allowing a mortality rate at a given age to depend on current and past GDP levels leads to estimates that are potentially very sensitive to small model misspecifications. For example, if the postulated relation is log-linear in the mortality rate and current GDP, and the true relation is slightly different, then this may show up as a significant effect of GDP earlier in life.

The effects of short-term cyclical movements in GDP are not affected by secular improvements. Still, because of the gradual secular improvements over time, being born in a later stage of the cycle entails that the individual will live under somewhat

[4] See Andreev 2002; Johansen 1985, and National Board of Health 1983 for detailed descriptions of demographic developments in Denmark in our observation window, including aggregate cause-of-death information.

better current conditions at each age. As a conservative strategy, one may compare a cohort born in a boom with the cohort born in the subsequent recession because the latter benefit more from secular developments than the former, so that an observed increase of a mortality rate can be attributed to the cyclical effect. More generally, one may relate a mortality rate later in life to the state of the business cycle early in life for many different birth years.

The raw GDP data are from Mitchell (2003). We deflate this nominal time series by using the price index series of Johansen (1985) and Mitchell (2003).[5] Next, we perform a trend/cycle decomposition of log annual real per capita GDP, using the Hodrick-Prescott (HP) filter. We use smoothing parameter 100, which ensures that the time series of the cyclical component (or deviation) of GDP does not display a trend over the interval of birth years that we consider. The values of the cyclical terms are robust with respect to the actual decomposition method and smoothing parameter, and so are the resulting intervals within which the terms are positive or negative. In sum, good and bad transitory macroeconomic conditions are clearly identifiable in the data.

Figure 1 displays the cycle and trend as functions of calendar time. We have 17 years with a positive cyclical component and 17 with a negative. The average number of consecutive years in which this component does not change sign equals 2. Among years with a positive (negative) component, this number is 1.9 (2.1).

Some Direct Data Evidence

The Business Cycle at Birth, Longevity, and CV Mortality

It is useful to start listing some sample features that should be kept in mind in the statistical analysis of sample descriptives. First, within-twin pair outcomes are related because of shared determinants. We cannot use within-pair outcome differences to study long-run effects of macro conditions because the latter conditions are identical for both twins. Moreover, because of shared or related determinants, the sample of individual twins is not a sample of *independent* draws from the distribution of individual lifetimes of twins. This is exacerbated by the requirement that both twins be alive in 1943. Randomly discarding one individual per observed twin pair would complicate the selectivity in the sample of individuals because survival of the co-twin until 1943 depends on the twin-specific frailty and on early-life conditions and their interactions.

With this in mind, consider first the mortality from all death causes. Because of the left-truncation of lifetimes in 1943, we cannot simply compare the observed average lifetime durations across different birth cohorts, even if we would aggregate booms and recessions and even though the cyclical indicator is orthogonal to any trends. After all, the left-truncation point varies across birth years. To proceed, we examine the mean lifetime duration $\mathrm{E}(T \mid T \geq 70,\ \tau_0)$, conditional on the age T exceeding 70, among those born in birth year τ_0. We estimate this as the mean

[5] All time series used in this article, including descriptions of their origin and/or construction, are available upon request.

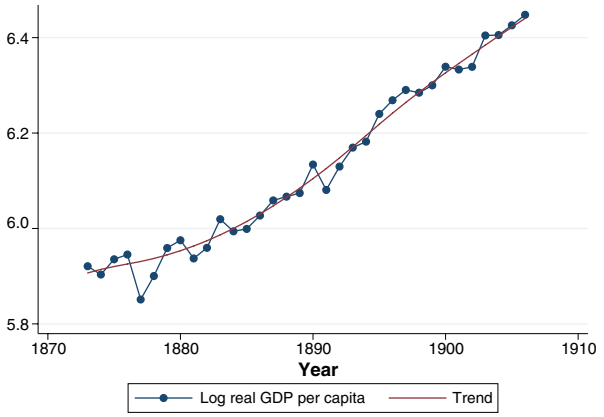

Fig. 1 Log real GDP per capita: Trend and cycle

lifetime among uncensored lifetimes among those born in τ_0 who survive until age 70, for each birth year. Subsequently, we obtain the deviation in the time series of E $(T \mid T \geq 70,\ \tau_0)$ in order to remove the trend in longevity, and we correlate this deviation variable with the business cycle indicator at τ_0. Figure 2 displays the two time series.

To interpret the displayed values, recall that the GDP cycle represents the percent deviation of annual real per capita GDP from its trend value. The deviation of the mean conditional lifetime is measured in 10^4 days; thus, a deviation of 0.018 corresponds to 6 months.

The figure suggests a positive association, and the estimated correlation between the two time series equals .3. This provides some evidence that the business cycle at birth has a negative effect on the mortality rate at higher ages. The mean lifetime among those born in years in which the business cycle component is positive is 6.5 months higher than when born in the other years, conditioning on $T \geq 70$. Formal statistical tests lead to the rejection of equality of these means at conventional levels of significance.

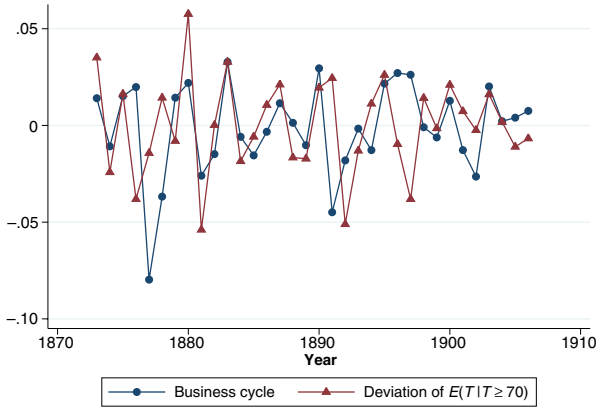

Fig. 2 The business cycle and the transitory component in the mean lifetime in the birth cohort (conditional on survival until age 70)

The preceding approaches that consider moments of lifetimes cannot be used for CV mortality because the duration until death from CVD is often right-censored by death from other causes. However, by assuming that all other death types constitute independent right-censoring of the duration until CV mortality, we can nonparametrically estimate the CV mortality rate, distinguishing by whether the business cycle component in the birth year is positive. Specifically, we use the Ramlau-Hansen kernel estimator for hazard rates (see, e.g., Andersen et al. 1993). Figure 3 displays the estimates based on a kernel bandwidth of 3 years. Clearly, at most ages, the CV mortality rate is higher if born in an adverse birth year. The estimated median of the duration until CV mortality, conditional on survival until age 36, equals 83.9 years if one is born in a "bad" year and 85.6 years if one is born in a "good" year.

Estimation of Duration Models for the Individual CV Mortality Rate

Models for Individual Mortality Rates

Basic Model Specification

The individual (CV) mortality rate is the natural starting point of the specification of the model because of our interest in its dependence on conditions early in life. Because our model specifications closely follow those in the literature, the present exposition can be brief. Age is measured in days, so we take it to be a continuous random variable. Let τ denote current calendar time. We may express the (CV) mortality rate θ of an individual at a given point of time in terms of the prevailing age t, individual background characteristics x, current conditions $z(\tau)$, exogenous business-cycle indicators $c(\tau-t)$ of early-life conditions, unobserved characteristics or frailty V, and various interaction terms. For example,

$$\log\theta(t|x,z,c(\tau-t),V) = \psi(t) + \beta_1'x + \eta'c(\tau-t) + \beta_2'z(\tau) + \log V, \qquad (1)$$

where η is the parameter of interest. We capture long-run secular and current trend effects $z(\tau)$ by way of a low-order polynomial in the log birth year.

In the absence of unobserved heterogeneity, the model reduces to a proportional hazard (PH) model, and the parameters β and η can be estimated with partial likelihood estimation. Absence of unobserved heterogeneity implies independence of the within-twin pair lifetimes conditional on the covariates x, the (shared) early-life conditions, and the secular effects as captured by the birth year. The partial likelihood approach thus tackles at least part of the unconditional dependence of within-pair lifetimes.

Implications of Ignored Heterogeneity Among Newborns and Evidence on the Lack of Compositional Changes

Unobserved heterogeneity among newborns that is not taken into account in the estimation can bias the estimates of long-run effects of early-life conditions. We

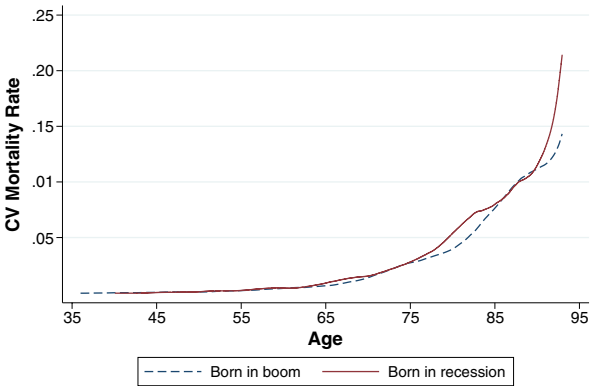

Fig. 3 Nonparametric estimates of the CV mortality rate by whether the cycle at birth is larger or smaller than 0

distinguish between within-cohort heterogeneity on the one hand, and systematic between-cohort variability in the composition of newborns on the other.

To address the effect resulting from within-cohort heterogeneity, notice that covariate effects on the hazard rate are typically biased toward zero if unobserved heterogeneity is ignored (see van den Berg 2001 for an overview of the literature). Recall that we observe lifetime durations only if they exceed the twins' ages in 1943. With unobserved heterogeneity, dynamic selection may lead to an overrepresentation of high-age survivors with favorable characteristics, among those born in adverse years (see, e.g., Vaupel and Yashin 1985 for details). Thus, if unobserved heterogeneity is present but is not taken into account, then the coefficient η of the indicator of early-life effects can be expected to be biased toward zero, and the true effect is likely to be at least as large in absolute value. This also applies to the effects of a possible increase in stillbirths and spontaneous abortions during adverse conditions.

This problem may be less relevant than in other studies of effects of early-life conditions on mortality much later in life. Among all countries and all eras up to the twentieth century, Denmark had the lowest infant mortality ever. Alternative indicators of early-life conditions focusing on extreme events such as epidemics or famines may lead to peaked infant mortality and strong ensuing dynamic selection of the fittest in the cohort.

Another implication of within-cohort variability is that most likely, it leads to statistical dependence of twins' lifetimes. After all, the lifetimes of both will be affected by shared characteristics that are not among the observed covariates x. Failure to take this dependence into account may lead to underestimation of coefficient standard errors. We therefore also estimate models allowing for unobserved heterogeneity in personal and environmental characteristics (see the section Correlated Frailty Model).

We now turn to between-cohort variation in the distribution of unobservable personal characteristics. It is conceivable that the distribution of CV-mortality determinants among newborns varies over the cycle. A long-run association between the business cycle at birth and high-age mortality can be explained if parents with adverse unobserved permanent characteristics (such as a low social class) more often have offspring during recessions. We investigate this in two ways. First, we examine fluctuations in cohort sizes, following the idea that systematic variation in cohort

size leads one to suspect systematic changes in the composition. For example, Saugstad (1999) showed that in Denmark, changes in the composition of newborns go along with changes in birth rates. Second, we discuss direct evidence on the composition. This includes an examination of the fraction of twins itself among newborns. Online Resource 1 provides details. We conclude that fertility is independent of the contemporaneous state of the business cycle, that the fraction of twin births does not vary sizably across the business cycle, and that the composition of newborn twins in terms of social class, education, and other personal characteristics does not vary systematically over the business cycle. Other studies with data from northwest Europe from around 1900 also fail to find that the social-class composition of newborns is systematically related to fluctuations in macro indicators early-life conditions (Kåreholt 2001; van den Berg et al. 2009).

Correlated Frailty Model

To incorporate unobserved heterogeneity, we adopt the correlated gamma-frailty model, which is often used in demography to study twins' lifetimes (see, e.g., Wienke et al. 2001, 2002). This model postulates that the within-twin pair frailty terms follow a Cherian bivariate gamma distribution. It allows for an interpretation of the individual frailty term as the sum of an individual-specific term and a shared twin-specific term. The shared term W captures shared genetic determinants and relevant features of the shared environment in which the twins lived. The individual-specific term V^0 captures individual-specific characteristics that are not shared with the co-twin. As a result, the joint distribution of V_1,V_2 has two parameters: the variance σ^2 of V_i, and the correlation ρ of V_1 and V_2 (see Online Resource 1). The latter equals the fraction of the total variance of V explained by W,

$$var(V_1, V_2) = \rho = \frac{var(W)}{var(V_i)}.$$

For our purposes, we need to parameterize the age-dependence function ψ in the correlated gamma frailty model. We assume that this is a Gompertz function: that is, $\psi(t)=\alpha t$. With lifetime durations of older individuals, this functional form is not controversial and is known to give an acceptable fit to age dependence in many cases.

We estimate the correlated frailty models by maximum likelihood, using the GAUSS program, taking account of the left-truncation of both twins' lifetimes at the age reached in 1943 and taking account of right-censoring due to missing information on the death date and right-censoring due to death being caused by another cause (for expressions of the full likelihood function, see Wienke et al. 2002; statistical estimation programs are available upon request).

Estimation Results

Table 1 gives the partial likelihood estimates of the most basic Cox PH model specifications. The estimates concern the CV mortality rate, so a positive value is associated with a shorter CV lifetime. The binary "recession at birth" indicator captures macro-level fluctuations around birth. One of the specifications has a more

Table 1 Cox partial likelihood parameter estimates of proportional hazard models for the individual CV mortality rate

Variable	Parsimonious		Extended	
	Estimate (SE)	*t* Value	Estimate (SE)	*t* Value
Recession at Birth	0.12 (0.037)	3.2	0.12 (0.037)	3.2
Male	0.33 (0.037)	8.9	0.34 (0.037)	9.0
Log (birth year – 1872)	–0.094 (0.030)	3.1	–0.090 (0.030)	3.0
Season				
Spring	0.12 (0.043)	2.8	0.050 (0.052)	1.0
Summer			–0.076 (0.051)	1.5
Winter			–0.14 (0.051)	2.7
Birth Location				
Copenhagen	0.15 (0.056)	2.6	0.15 (0.059)	2.6
Town			0.012 (0.051)	0.2
Zealand			0.014 (0.044)	0.3
Funen			0.012 (0.061)	0.2
MZ	–0.039 (0.038)	1.0	–0.041 (0.038)	1.1
Log Partial Likelihood	–22,496.9		–22,493.2	

Note: In the extended specification, the default birth location is rural in Jutland.

parsimonious set of covariates than the other. In both specifications, being born in a recession increases the CV mortality rate by 12%. The estimate is strongly significant. This is the first main result of the article, and as we shall see, this finding is robust to many departures from the basic model specifications. The result implies a significant causal effect of economic early-life conditions on CV mortality much later in life, and as such, it bridges the gap between the economic and medical literatures. All results are robust with respect to the measure used to capture the business cycle in the birth year.

The implied causal effect of the business cycle at birth on the mean lifetime conditional on $T \geq 40$ is as follows. If an individual is born in a boom as opposed to a recession, then one can expect to live 0.8 years longer beyond age 40 just because the risk of CV mortality is lower.

The effects of birth season are in accordance to those reported in Doblhammer (2004) based on a larger set of Danish twins. A likelihood ratio (LR) test confirms joint significance of seasonal effects (p value = .002). The CV mortality rate is not significantly different between MZ and DZ twins. This is a common finding if one restricts attention to twins surviving infancy (see, e.g., Christensen et al. 1995; and Wienke et al. 2001).

According to an LR test, the parsimonious specification does not give a worse fit than the extended specification (p value = 0.19). We have two reasons for working with the parsimonious set of covariates. First, maximum likelihood estimation of correlated frailty models becomes cumbersome if the number of covariates is large, particularly if we allow the parameter ρ to depend on x and the value of ρ is close to (or equals) 1 or 0 for some values of x. Second, we want to assess the sensitivity of

the results with respect to a wide range of model assumptions, and these results are more easily discussed for a parsimonious specification.

Table 2 displays the maximum likelihood estimates of the correlated gamma frailty model. The covariate effects (notably, the "recession at birth" coefficient) are similar in sign, relative magnitude, and significance to the Cox PH specification in Table 1.

The correlation coefficient for MZ twins always exceeds the coefficient for DZ twins. In fact, the estimated correlation for MZ twins is at the upper boundary (i.e., at 1) of the parameter space. This estimate is not inconsistent with a true parameter value smaller than 1, but it is not possible to test whether the parameter is equal to 1 because there is no standard error associated with an estimate at the boundary.

The estimated correlation ρ for DZ twins equals .85 if born in a recession (with standard error 0.17) and .49 if born in a boom (with standard error 0.0085). The fact that the former standard error is much larger than the latter merely reflects the fact that the likelihood function is very flat in ρ for values of ρ close to 1. We reject the null hypothesis that states that within-pair lifetimes for DZ twins do not depend on early-life conditions. The difference between the estimated correlations equals .36, and this is significantly different from zero at the 5% level, as the standard error of the difference (estimated with the multivariate delta method) equals 0.17 (so the t value is 2.2). Alternatively, we may use an LR test. Estimation of the restricted model in which the correlation for DZ twins does not depend on the cycle at birth results in a point estimate of .65 for this correlation. The LR test statistic equals 2.8,

Table 2 Parameter estimates of the correlated gamma frailty model for the individual CV mortality rate

Variable	Estimate (SE)	t Value
Covariates		
Recession at birth	0.14 (0.050)	2.8
Male	0.45 (0.052)	8.8
Log (birth year – 1872)	–0.12 (0.044)	2.7
Spring	0.16 (0.058)	2.7
Copenhagen	0.18 (0.075)	2.3
MZ	–0.033 (0.051)	0.6
Gompertz Age Dependence	0.000371 (0.00001)	40.5
Bivariate Frailty Distribution		
Variance	0.49 (0.063)	7.9
Correlation DZ Recession	.85 (0.17)	5.1
Correlation DZ Boom	.49 (0.0085)	57.7
Correlation MZ Recession	1	
Correlation MZ Boom	1	

Notes: The correlation parameter of the bivariate frailty distribution is the correlation between the unobserved CV mortality determinants of the two twins within a twin pair. It also allows for an interpretation as the fraction of the total individual variation in unobserved CV mortality determinants that is shared with the co-twin. By "unobserved determinants," we mean the factor in the CV mortality rate that captures the joint effect of all unobserved explanatory variables. The table lists estimates of separate correlation parameters for all four combinations of zygosity and state of the business cycle at birth.

which is significant at the 10% level. We now turn to the interpretation of the estimated correlation coefficients.

Correlated gamma frailty models that are estimated with twin data can be used to decompose variation in the outcome into components reflecting genetic, environmental, and individual-specific terms (see, e.g., Wienke et al. 2002 for a detailed exposition). For a given zygosity, the nonshared variation in the frailty term captures variation due to unobserved individual-specific determinants, whereas the shared variation captures variation in unobserved shared genetic determinants and variation in the unobserved shared environmental determinants, such as conditions of the household in which the twins grow up. We may compare the relative magnitudes of these variations by zygosity and by early-life conditions.

Our estimates for MZ twins are not very informative in this respect because they are at the boundary of the parameter space. The estimates for DZ twins imply that shared genetic and environmental factors are more important for CV mortality if the individual is born under adverse economic conditions. Individual-specific factors dominate stronger if the individual is born under better conditions.

This dependence of the importance of shared genetic and environmental factors on conditions at birth is an interesting result. In short, individual-specific qualities come more to fruition if the starting position in life is better. Individuals who possess unique features protecting them against CVD will not benefit so much from them if they are born under adverse economic conditions. If one interprets the business cycle itself as an environmental factor, then one may formulate the conclusion that nature and nurture interact in their effect on CV mortality.

Underlying Mechanisms

Critical Months Around the Birth Date

Naturally, the medical and epidemiological literature explains the relation between birth weight indicators and CVD later in life by way of conditions *in utero*, notably the nutritional intake of the mother. The same applies to much of the other literature on early-life conditions, including studies exploiting famines or the season of birth, in which sometimes the variation in the moment of onset of adverse conditions can be used to identify the subset of the gestational period that matters most. Often, the results are consistent with the hypothesis that (nutritional) conditions during the last three months of pregnancy are a pivotal determinant of CVD later in life (see the overviews cited in the first section and references therein). There are also studies that focus on conditions at or after birth, including studies that exploit variation in infant mortality rates to identify long-run effects of disease exposure shortly after birth, and studies that exploit variation in household circumstances around birth (again, see the first section).

Our data allow us to shed more light on the relative importance of conditions in the months before and shortly after birth, and thus on the underlying mechanisms by which adverse economic conditions affect CVD later in life. We effectively exploit the facts that (1) the business cycle in the years before and after the birth year varies across individuals, and (2) we observe the precise birth date within the birth year.

This allows us to identify critical periods around the date of birth. For example, the effect of conditions in the month prior to birth can be identified by using variation in the business cycle indicator values in the month prior to birth across individuals born in January in different years. Similarly, data on individuals born in December can be used to obtain the effect for the month after birth. However, it is not feasible to estimate a single model with separate indicators for (1) a given fixed number of months prior to (or after) birth and (2) an indicator for the day of birth: for most individuals, such indicators have the same value because they are not born at the extremities of the calendar year. In addition, GDP is measured at a yearly frequency, making GDP a potentially less-accurate measure of macroeconomic conditions at the year's extremities than in the middle of the year. For these reasons, we adopt a different approach that leads to a direct visualization of the effects. Consider the individual time intervals from the birth date to m months before or after it ($m = -12, -11, \ldots, -1, 0, 1, \ldots, 11, 12$). These are 25 different intervals I_m. For each value of m, we calculate the average observed business cycle indicator over the interval I_m. Subsequently, we estimate separate versions of the parsimonious model of CV mortality, where the average indicator replaces the indicator in the birth year as an explanatory variable. This results in 25 model estimates. Figure 4 displays the coefficients of the average indicator in the interval I_m as a function of m. The larger the coefficient, the stronger the long-run effect of conditions in the interval I_m on the CV mortality rate later in life.[6] Of course, the coefficient at $m = 0$ is the estimate from the first column of Table 1.

Clearly, the largest values are obtained for the intervals that end one or two months before birth, indicating that what matters most are the economic conditions during the final two months during pregnancy. The latter agrees very closely to results in the aforementioned medical literature, and as such, it confirms that the nutritional intake of the mother during the final months of pregnancy is a determinant of CVD at higher ages. Most likely, the economic conditions affect the quality of nutrition that the mother consumes in these months, which in turn affects the physical features of the child that are of importance for the likelihood of developing CVD at higher ages.

Spatial Variation in the Effect Size

To obtain further insights into the underlying mechanisms, we interact the business cycle at birth with regional indicators and the degree of urbanization. To interpret the results, we use historical studies of living conditions in Denmark in the nineteenth century, notably Løkke (2002), Johansen (2002a, b), and Henriksen (2006), and references therein.

We start by interacting the recession indicator with the urbanization variable. For the full sample, it turns out that the recession effect does not vary with the degree of urbanization (i.e., it is virtually equal over towns, rural areas, and Copenhagen). The same applies to the recession effect by region. However, the historical literature suggests that urbanization may play a different role in different regions owing to

[6] The figure is essentially the same if we average over the actual transitory component of log annual real per capita GDP instead of over the binary indicator.

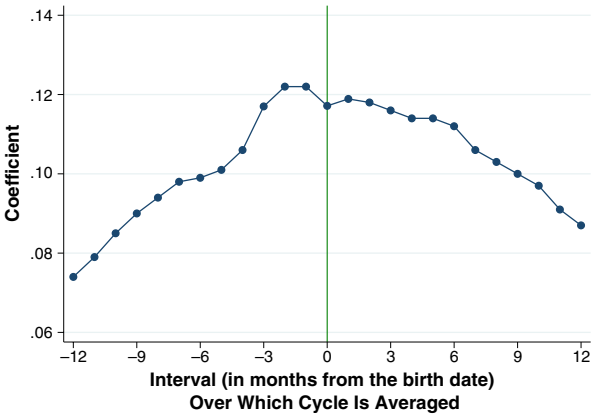

Fig. 4 Estimates of long-run effects of the business-cycle indicator on the individual CV mortality rate, where the indicator is averaged over intervals from the birth date to months ranging from −12 to 12 months

differences in nutritional habits across regions (see, in particular, Løkke 2002). We therefore proceed by estimating models on the subsample of those born on the island of Zealand (which includes Copenhagen). This region is relatively small, and it displays the highest variation in the degree of urbanization. For this subsample of 2,262 individuals, the coefficients of the basic model without interactions are very similar to those in Table 1. In particular, the recession at birth has a coefficient of 0.14 ($t = 2.4$), while "Copenhagen" and "town" have coefficients of 0.15 ($t = 2.2$) and 0.03 ($t = 0.3$), respectively. As before, these additive urbanization coefficients cannot be interpreted as long-run effects because they also reflect instantaneous effects at higher ages.

Table 3 provides the estimates of the model for Zealand and Copenhagen with interactions between the recession and urbanization indicators (note that the sample size is about one-third that in the other tables). Clearly, recessions at birth have the strongest adverse effects in towns (coefficient = 0.34, with t value = 2.1), whereas the effects in Copenhagen and in rural areas are in line with the national estimate. By implication, birth in a town during a recession leads to the same CV mortality rate later in life as birth in Copenhagen during a recession, whereas in a boom year, it is much more advantageous to be born in a town. From the historical literature, a plausible explanation for the difference between the size of the interaction coefficients is that in Copenhagen, the sanitary conditions and the health care system were superior to those in other towns (see also Lindegaard 2001 for the history of the sewerage system). For example, Copenhagen was equipped with a large special hospital for deliveries and provided clean milk to infants after breastfeeding. In towns during recessions, the effects of inferior nutrition on the mother's and infant's health status could not be mitigated by good sanitary conditions or health care access. In rural areas, sanitary conditions were not as inadequate as in towns, while access to nutrition was easier than in towns.

The results in Table 3 and their explanation suggest that the combination of nutritional quality and health infrastructure is important for long-run effects of early-life conditions: if both nutritional quality and health infrastructure are

Table 3 Parameter estimates for the individual CV mortality rate in Zealand, including Copenhagen, with interactions between cyclical and urbanization indicators

Variable	Estimate (SE)
Recession at Birth in Copenhagen	0.14 (0.11)
Recession at Birth in Town	0.34* (0.16)
Recession at Birth in Rural Areas	0.10 (0.082)
Male	0.38* (0.061)
Log (birth year – 1872)	–0.12* (0.049)
Spring	0.11 (0.071)
Birth Location	
Copenhagen	0.13 (0.089)
Town	–0.087 (0.13)
MZ	–0.021 (0.063)

Note: The sample is the subsample of those born in Zealand, including Copenhagen (sample size = 2,262).
*Significant at the 5% level.

lacking, then high-age CV mortality is relatively strongly affected. Along this line of reasoning, adverse economic conditions leading to suboptimal early-life nutritional patterns are more harmful in the long run if the health infrastructure close to the moment of birth is inadequate. Of course, we also find long-run effects for those born in areas where both features are not lacking. These may capture a separate long-run effect of nutrition and a separate long-run effect of sanitation and health care. In any case, these effects are smaller than one-half of the effect for areas where both are lacking.

It is possible that the causal pathway from economic conditions to CV mortality at higher ages is amplified by stress at the household level shortly before and/or shortly after birth. Adverse aggregate conditions may induce stress by way of (a higher perceived probability of) income loss. Moreover, stress may exacerbate the effects of adverse nutrition and health infrastructure by the perception that nutrition and health care will be insufficient. Farah et al. (2008) found that poverty in the household leading to stress causes neurological damage among children in the first years of their life, resulting in a lower IQ.

We briefly consider some other possible explanations. If inferior housing conditions with inadequate heating and crowdedness were a major factor, then one would expect the business cycle effect among those born in Copenhagen to exceed the corresponding effect among those born in rural areas. The same applies to exposure to job loss. In fact, crowdedness seems to have been particularly high in towns in boom years, as many workers from rural areas then migrated temporarily to towns. Epidemics were virtually absent during our observation window. Thus, exposure to diseases does not seem to be a primary explanation of our results, either.

Finally, if Copenhagen were more heavily exposed to the business cycle than other parts of the country, then the cyclical effect should be larger among those born in Copenhagen than among those born elsewhere. The historical literature points out that other towns were as industrialized as Copenhagen.

Effects for the Other Death Causes

We replicate the analysis of the CV mortality rate for a range of other mortality rates. First, we consider the overall mortality rate for all causes and the mortality rate from cancer. Next, we consider a range of less-common death causes: notably, various types of infectious diseases. We finish by decomposing CV mortality into different subcategories. The main results are summarized in Table 4.

Clearly, the cycle at birth has a significant effect on the overall individual mortality rate later in life. The coefficient in the overall mortality rate is slightly smaller than the coefficient in the CV mortality rate, but the effect on overall lifetime durations is larger than if the long-run effect would work only through CV mortality. Specifically, the causal effect of the business cycle at birth on the mean lifetime conditional on $T \geq 40$ is such that being born in a boom as opposed to a recession results in 1.25 additional years. This result is similar in magnitude to the result in van den Berg et al. (2006) for the effect of the business cycle at birth on longevity among those who survive infancy in the Netherlands in the birth cohorts 1815–1902.

We now turn to the cause-specific rates. To prevent that the results are driven by only a few observations, we consider relatively broadly defined death-cause categories, and we consider only those categories that occur in more than 3% of the full sample. Moreover, we assume that in the analysis of a given death cause, death from any other cause can be treated as independent right-censoring conditional on the explanatory variables. As mentioned earlier, the independent censoring assumption has been confirmed in some cases, but it is unlikely to hold true if the death cause of interest is a specific infectious disease because mortality from all infectious diseases may be driven by common determinants of the immune system. Table 4 presents the estimates of the business cycle indicator on the cause-specific mortality rates, where in all cases, we use a Cox PH model specification with the parsimonious set of explanatory variables.

First, the business cycle at birth does not have a significant effect on the cancer mortality rate (cancer is the death cause for 21% of the sample). The sign of the coefficient is positive, suggesting higher cancer incidence for those born under adverse conditions, but the magnitude is very small compared with the coefficient for the CV or

Table 4 Estimated effect of recession at birth on the overall mortality rate, on the mortality rates for non-CV death causes, and for subcategories of CV mortality

Death Cause	Observed Frequency in the Sample (%)	Estimate (SE)	*t* Value
All Causes	100	0.093 (0.027)	3.5
Cancer	21	0.032 (0.059)	0.6
Infectious Diseases	14	0.13 (0.073)	1.9
Respiratory	7	0.14 (0.10)	1.4
Digestive	3	–0.084 (0.15)	0.5
Accidents	4	–0.11 (0.14)	0.8
CV Subcategory: CHD	35	0.14 (0.045)	3.2
CV Subcategory: CVA	18	0.065 (0.064)	1.0

Each line is based on a different model estimation. Estimates of the other model parameters are not shown.

the overall mortality rate. In fact, the medical evidence does not lead us to suspect that the overall cancer mortality rate late in life is higher in case of adverse economic conditions around birth. Ahlgren et al. (2007) demonstrated positive associations between birth weight and the rates at which almost all types of cancer occur at higher ages. By analogy to the negative association between birth weight and CVD, a positive association between birth weight and cancer at higher ages actually suggests that improved economic conditions at birth might lead to a higher rate of certain cancers.

There is some evidence to date suggesting that birth under adverse conditions increases high-age mortality from infectious diseases. For example, Bengtsson and Lindström (2003) showed that individuals born during smallpox or whooping cough epidemics die more often from airborne infectious diseases later in life. Kuh and Ben-Shlomo (2004) surveyed studies reporting an association between birth size measures and respiratory diseases later in life. Our own results provide evidence for a long-run effect of economic conditions early in life on mortality from infectious diseases. The coefficient is of the same order of magnitude for CV mortality. It is significant at the 10% level. This result demonstrates that the effect of economic conditions early in life on overall mortality later in life is not only revealed in CVD. We do not find an effect on higher-age mortality from infectious diseases of the digestive system. Perhaps not surprisingly, there is also no effect on death from accidents.

Finally, we consider subcategories of CV mortality. In line with common practice (see, e.g., Lawlor et al. 2004), we distinguish between two subcategories: death from coronary heart disease (CHD, or ischemic heart disease) and death from strokes (cerebrovascular accidents, or CVA). We define these subcategories relatively broadly, such that they are exhaustive for CVD.[7] However, the most common types of diseases in our CHD and CVA subcategories are also the most common types in the more-narrow CHD and CVA typologies often used in the literature (see, e.g., Koupil et al. 2005). Further disaggregation would lead to incompatibility issues of the different ICD revisions used in the data. Moreover, the specific death causes within the CHD and CVA subcategories may often have a common cause, making it questionable to assume independent right-censoring in analyses for a given death cause within such a subcategory.

Lawlor et al. (2004) surveyed the overwhelming evidence on the association between birth-size versions on the one hand, and fatal and nonfatal CHD and CVA on the other. The evidence for CHD is particularly strong. In Table 4, we report the effects of economic conditions at birth, and indeed, it appears that the effect on CV mortality rate is mostly driven by the effect on CHD mortality. The latter coefficient is somewhat larger than in Table 1 and is highly significant. Conversely, the coefficient for CVA mortality is smaller and insignificant.

Conclusions

Transitory macroeconomic conditions at birth have a significant effect on the cardiovascular mortality rate much later in life. An individual who is born in a

[7] In terms of ICD revision 8, our CHD subcategory contains codes 394–429, and our CVA subcategory contains 290, 430–441, and 794.

recession and who survives until age 40 lives around 11 months shorter than an otherwise identical individual born in a boom just because the risk of CV mortality is lower. This implies that economic conditions around the time of birth have a negative causal effect on cardiovascular mortality later in life.

From temporal variation in the effect, we deduce that among all months in the year prior to the birth date and in the first year of life, the last months of pregnancy are the most pivotal in the sense that economic conditions in those months matter most for long-run CV mortality. This finding suggests that the nutritional intake of the mother during the final months of pregnancy is a determinant of CVD at higher ages. From spatial variation in the effect, we deduce that effects of nutritional quality interact with the quality of health infrastructure in the sense that economic conditions leading to suboptimal early-life nutritional patterns are more harmful in the long run if the health infrastructure early in life is inadequate. The results do not point at important roles for disease load exposure or housing conditions.

For cancer-related mortality, we do not find long-run effects of early-life conditions. Mortality from infectious diseases does seem to be affected by early-life conditions, and this is especially true for diseases of the respiratory system. The effect on CV mortality seems to be driven mostly by an effect on coronary heart diseases rather than on strokes.

The results for the long-run economic effects on CV mortality rates are in accordance with the medical and epidemiological literature. Because the latter are based mostly on associations between birth weight and health later in life, we feel that the current study provides an important external confirmation of the "developmental origins" literature concerning cardiovascular diseases. At the same time, the fact that so many of our results on cause-specific mortality rates are in agreement to the medical and epidemiological literature lends credence to our analyses as well.

Our data on twins allow us to assess the extent to which variation in cardiovascular mortality can be attributed to genetic and household-environmental factors on the one hand, and individual-specific factors on the other. It turns out that genetic factors are more important if the individual is born under adverse economic conditions. Conversely, if the individual in born under better conditions, then individual-specific factors dominate more. In short, individual-specific qualities come more to fruition if the starting position in life is better. Because the extent to which genetic factors express themselves depends on the environment into which an individual is born, one may argue that nature and nurture interact in their effect on cardiovascular mortality. This is by no means the first study to report such an interaction. However, by using exogenous indicators of economic conditions early in life, we are at a methodological advantage over studies using family income or social status as an interacting variable for genetic determinants.

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